

Case Report

Successful treatments for allergic bronchopulmonary aspergillosis in non-cystic fibrosis children: a report of two cases and a literature review

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Abstract: Allergic bronchopulmonary aspergillosis (ABPA) is a disease induced by an exaggerated immune response to *Aspergillus fumigatus*, often occurring in susceptible adult patients with asthma and cystic fibrosis (CF). Proper treatments can alleviate symptoms, reduce pulmonary infiltrates and prevent progression of lung destruction. However, treatment experiences in ABPA children without CF are limited. Here we present two cases of successful treatments of ABPA in non-CF pediatric patients in China. We also present a literature review of ABPA treatments in 15 children without CF from 1971 to 2015. Based on these two cases, and our literature review, we recommend long-term low-dose oral corticosteroid therapy combined with antifungal agents along with close monitoring for these children, and suggest that anti-IgE therapy is not necessary.

Keywords: Allergic bronchopulmonary aspergillosis, cystic fibrosis, children, bronchiectasis

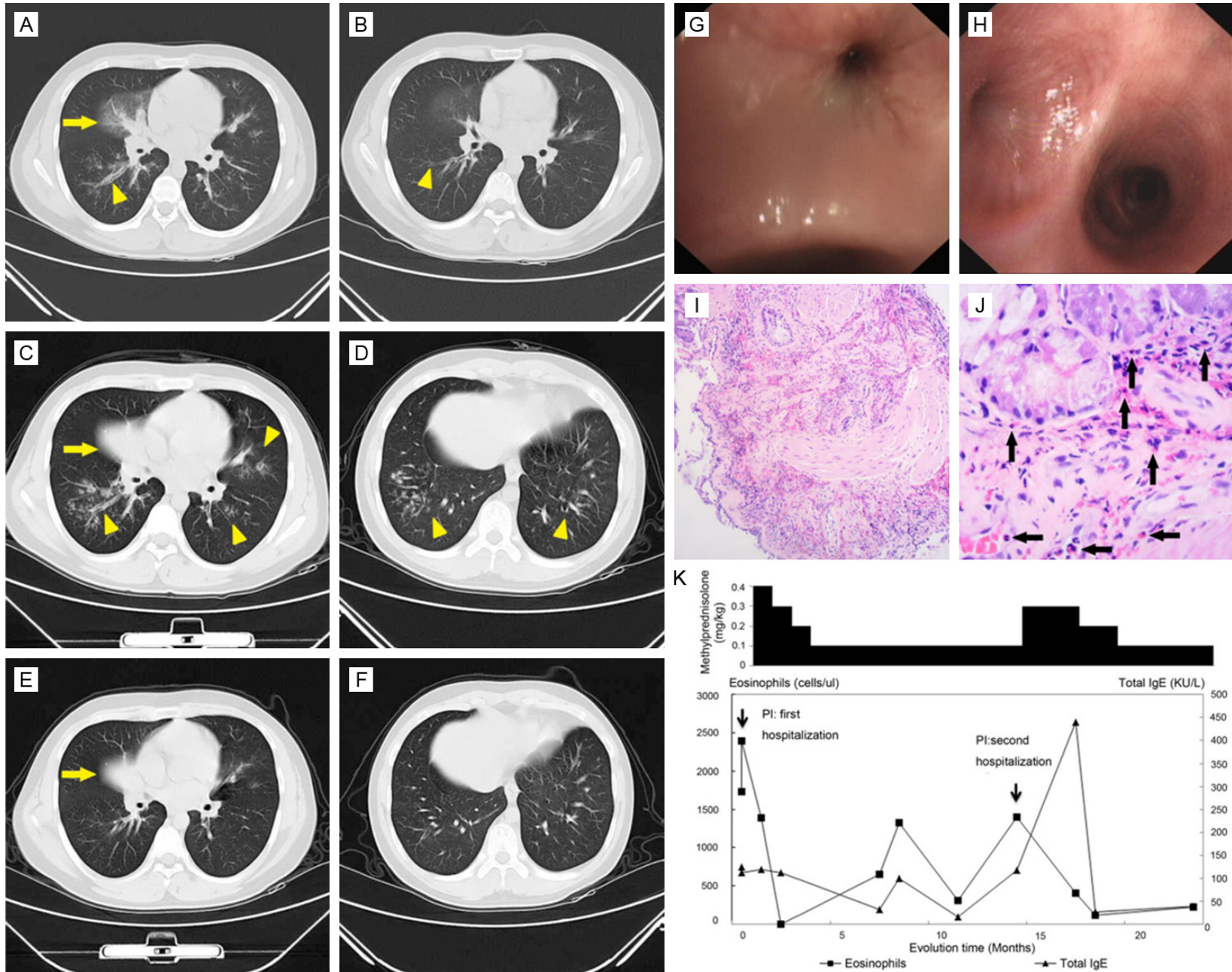
Introduction

Allergic bronchopulmonary aspergillosis (ABPA) is a complicated lung disease, which results from a hypersensitivity response to *Aspergillus fumigatus* (Af) colonization in the airways. It is predominantly seen in adults with asthma (2% to 15% of asthma patients) [1] and cystic fibrosis (CF, around 9% of CF patients) [2]. Common symptoms and signs include frequent cough with brownish mucus plugs, hemoptysis, wheezing, shortness of breath, chest pain, tightness and intermittent fever. Blood tests show a typical allergic reaction, including an extremely high level of total serum immunoglobulin E (IgE, usually more than 1000 ng/ml or 417 IU/ml), high levels of IgE and IgG antibodies that are specific to Af, and a peripheral eosinophilia. Skin testing for Af is often positive immediately [3]. However, some treatments, such as corticosteroids which are often used in asthma, can produce substantial declines in the levels of these serologic parameters and can therefore cause diagnostic difficulties. Chest X-rays are often not helpful in diagnosing ABPA, while a chest computed tomography (CT) scan with

higher resolution of the lungs is more useful. Diffuse infiltrates and central bronchiectasis are important findings that support the diagnosis [4].

If diagnosed in time and treated promptly, ABPA has a good prognosis. Corticosteroids are the most common and effective therapy and antifungals are added to reduce the Af antigen burden. In addition, anti-IgE drugs, such as omalizumab, may be an alternative therapy for ABPA in CF patients who have unacceptable adverse effects or respond poorly to systemic corticosteroids [5]. Omalizumab is a recombinant DNA-derived humanized IgG1 μ monoclonal antibody that selectively binds to human IgE thereby blocking IgE [6]. However, current treatment strategies for pediatric ABPA patients still need to be refined. There are two major problems: firstly, the efficacy and safety of the combination therapy of oral systemic corticosteroids and antifungals in children is unknown. Secondly, the role of anti-IgE targeted therapy is poorly understood. Although omalizumab has established efficacy in severe ABPA complicated CF, there are no double-blind, randomized,

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Figure 1. Case 1. A. Chest CT on admission showing infiltrates in the right middle lobe (yellow arrow) and central bronchiectasis in the right lower lobe (yellow triangle); B. Chest CT showing infiltrates absorbed 2 months later, remaining central bronchiectasis (yellow triangle); C and D. Chest CT showing new atelectasis in the right middle lobe (yellow arrow) and infiltrates in both lungs (yellow triangle) 14 months later; E and F. Chest CT showing a significant absorption of infiltrates in both lungs, but remaining atelectasis in the right middle lobe (yellow arrow) after treatments; G. Bronchoscopy examination showing mucosal swellings and orifice stenosis of the dorsal segment of the left lower lobe; H. Bronchoscopy examination showing the same changes 2 months later; I and J. H&E staining of biopsy tissue from the dorsal segment of right lower lobe showing mucosal chronic inflammation infiltrated with numerous eosinophils (black arrows were increased eosinophils), 100× (G1) and 400× (G2); K. Dose of methylprednisolone (Figure above), evolution of total serum IgE level and a peripheral blood eosinophil count (Figure below). PI, Pulmonary infiltrate (arrow).

placebo-controlled trials evaluating this treatment approach in ABPA patients without CF. Furthermore, omalizumab is an expensive therapy and it will be a huge waste of medical resources to promote widespread use of omalizumab if patients fail to have clinical benefit from anti-IgE therapy. Considering these two factors, anti-IgE therapy for non-CF children with ABPA needs to be carefully evaluated. In our report, we share our success in managing and treating ABPA in 2 non-CF pediatric patients. Also, we synthesize the limited published literature on treatments in ABPA children without CF, in order to provide some guidance for managing these patients.

Case reports

Case 1

A 17-year-old boy complained of recurrent episodes of cough and expectoration for more than 10 years. He was diagnosed with asthma at the age of 7, and required a combination of inhaled corticosteroids and short-acting β -agonists to control his respiratory symptoms. During several asthma exacerbations, he received short-term oral systemic corticosteroid therapy, resulting in a significant clinical improvement. Unfortunately, he frequently developed asthma exacerbations soon after discontinuing oral corticosteroids. He also had four surgeries for sinusitis and a family history of atopy.

On admission, the boy was in respiratory distress with normal arterial oxygen saturation. Auscultation of the chest revealed diffuse crackles in the right lung. Total peripheral blood eosinophil count was 2390 cells/ μ l (normal range 50-300 cells/ μ l), accounting for 20.6% of total peripheral blood cells (normal range 0.5-5%). Total IgE level was 113 KU/L (normal range 0-100 KU/L), and erythrocyte sedimentation rate was 52 mm/h (ESR, normal range 0-10

mm/h). Specific IgG and IgE against Af were 58 mg/L (positive, >50 mg/L) and 23.1 kUA/L (positive, >0.5 kUA/L), respectively. Skin prick test revealed positive and immediate reactions with Af. There was no mutation in CF transmembrane conductance regulator (CFTR) sequencing. Chest CT showed pulmonary infiltrates and central bronchiectasis in the right lung (**Figure 1A**). On bronchoscopy, significant mucosal swelling and orifice stenosis of the dorsal segment of the left lower lobe was identified (**Figure 1G**). Bronchoscopic lung biopsy tissue from the dorsal segment of the right lower lobe revealed eosinophilic inflammation (**Figure 1I, 1J**). Bronchoalveolar lavage examination was also carried out, and the proportion of eosinophils was significantly elevated to 18% in the bronchoalveolar lavage fluid (BALF). Lung function testing showed severe obstructive ventilatory dysfunction with a positive response to bronchodilation (FEV1: forced expiratory volume in one second 30% predicted; change in FEV1 over time 34%). The clinical diagnosis of ABPA was established and the patient was started on oral corticosteroids (methylprednisolone, 0.4 mg/kg/day) and oral itraconazole liquid (0.5 ml/kg/day), resulting in immediate improvements in respiratory symptoms and radiological infiltrates on a follow up CT scan 2 months later (**Figure 1B**). Another bronchoscopic examination was performed, but there were no significant changes (**Figure 1H**). His symptoms were stable and he was discharged when his oral systemic corticosteroids and itraconazole were being weaned. 3 months later, the itraconazole was discontinued and methylprednisolone was tapered to 0.05 mg/kg/day. Unfortunately, the boy was re-hospitalized for a severe exacerbation 14 months later. Chest CT showed new atelectasis in the right middle lobe and infiltrates in both lungs (**Figure 1C, 1D**). He was treated with oral itraconazole liquid (0.5 ml/kg/day) again and the oral methylprednisolone dose was increased to 0.2 mg/kg/day. He responded well to this therapy with improve-

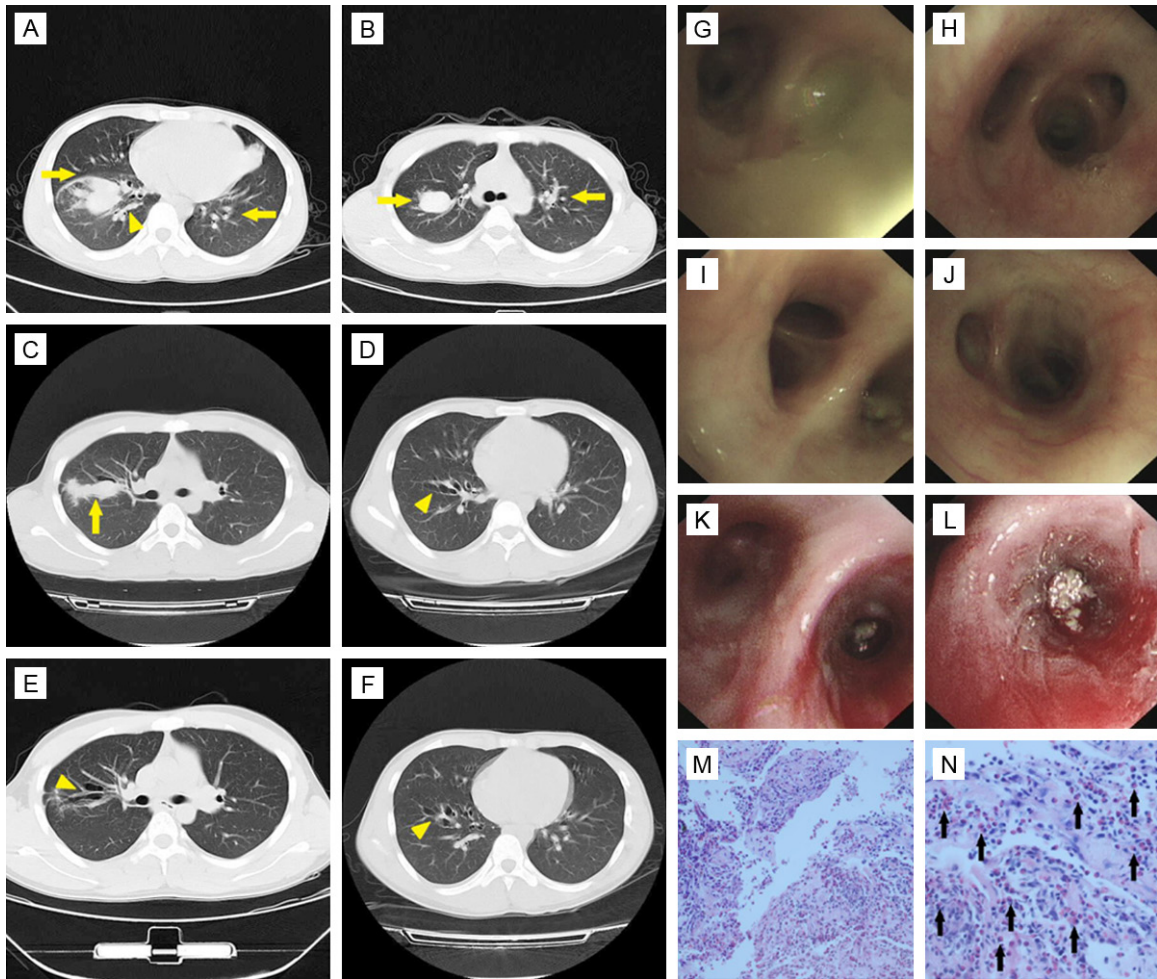


Figure 2. Case 2. (A and B) Chest CT at the first hospitalization showing pulmonary infiltrates in both lungs (yellow arrow) and a finger sign in the right lower lobe (yellow triangle); (C and D) Chest CT showing finger-like infiltrates in the right upper lobe (C, yellow arrow), along with cystic and columnar expansions in the right lung (D, yellow triangle) 15 months later; (E and F) Chest CT showing a complete absorption of infiltrates, remaining central bronchiectasis after discharge of sputum plugs (yellow triangle) 17 months later; (G-J) Orifice of both right lower lobe (G) and left upper lobe (I) were blocked by purulent sputum plugs on bronchoscopy during the first hospitalization and a clear airway was seen after removing sputum plugs (H and J); (K and L) Bronchoscopy examination showing anterior segment of the right upper lobe was blocked by a large amount of purulent sputum plugs 15 months later; (M and N) H&E staining of bronchoscopic lung biopsy tissues from the anterior segment of the right upper lung showing an eosinophilic abscess and necrosis (black arrows were increased eosinophils), 200× (M) and 400× (N).

ments in his whole blood cell count tests, total IgE level (**Figure 1K**) and chest CT (**Figure 1E, 1F**). The patient did not have any adverse events occurring during the subsequent 12-months and he received close follow-up with combination therapy of low-dose oral methylprednisolone (0.06-0.1 mg/kg/day) and itraconazole (0.3 ml/kg/day).

Case 2

A 15-year-old boy presented with a one-month history of intermittent low-grade fever and

cough with frequent passage of brownish plugs of sputum. He was diagnosed with asthma at age 5 years. There was no history of other diseases.

On admission, his eosinophil count was 1410 cells/ μ l (18.8%) and the total IgE level was 1165.0 KU/L. Serum Af-specific IgG and IgE were 62 mg/L and 15.3 kUA/L, respectively. The ESR was increased to 45 mm/h. The Af skin prick test was immediately positive. CFTR sequencing did not reveal any mutations. Chest CT showed pulmonary infiltrates in both lungs

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Table 1. Clinical profile of 15 ABPA pediatric patients without CF

Clinical characteristics	Results
Age, years	
Mean (SD)	12.8 (4.3)
Median (range)	13 (4.5-18.0)
Sex	
Male (%)	10/15 (66.7)
Female (%)	5/15 (33.3)
Symptoms	
Cough (%)	8/9 (88.9)
Expectoration (%)	6/9 (66.7)
Plugs (%)	4/9 (44.4)
Wheezing (%)	6/9 (66.7)
Dyspnea (%)	3/9 (33.3)
Chest pain (%)	2/9 (22.2)
Hemoptysis (%)	2/9 (22.2)
Fever (%)	7/9 (77.8)
Family history	
Asthma (%)	13/13 (100)
Rhinitis (%)	1/7 (14.3)
Atopy (%)	3/7 (42.9)
Laboratory data	
Positive skin reaction to Af (%)	12/12 (100)
Elevation of total IgE (%)	13/14 (92.9)
Elevation of total eosinophil count (%)	7/9 (77.8)
Imaging findings	
Pulmonary infiltrates (%)	10/15 (66.7)
Central bronchiectasis (%)	5/15 (33.3)
Treatments	
Oral systemic corticosteroids (%)	15/15 (100)
Maintenance systemic corticosteroids (%)	5/7 (71.4)
Intermittent systemic corticosteroids (%)	1/7 (14.3)
Discontinuity of corticosteroids (%)	1/7 (14.3)
Oral antifungals (%)	3/15 (20)
Maintenance antifungals (%)	2/2 (100)
Intermittent antifungals (%)	0
Discontinuity of antifungals (%)	0
Oral anti-IgE (%)	0
Drug side effects (%)	1/9 (11.1)
Clinical improvements (%)	11/11 (100)

and a finger sign in the right lower lobe (**Figure 2A, 2B**). Bronchoscopy showed a lot of purulent sputum plugs within the bronchi (**Figure 2G, 2I**) and a clear airway was seen after removing the sputum plugs (**Figure 2H, 2J**). In view of his recurrent respiratory exacerbations and large amount of mucus plugs, and serologic workup, a diagnosis of asthma complicated by ABPA

was made, but he refused any treatment. After 15-months of close monitoring, the boy complained about a recurrent cough productive of bloody sputum. Chest CT showed finger-like infiltrates in the right upper lobe, along with cystic and columnar expansions in both lungs (**Figure 2C, 2D**). These obstructive pneumonia-like changes caused by sputum plugs are classic for a typical presentation of ABPA. Meanwhile, bronchoscopy demonstrated a large amount of purulent sputum plugs within the right upper lobe (**Figure 2K, 2L**). Bronchoscopic lung biopsy tissues from the anterior segment of the right upper lung showed an eosinophilic abscess and necrosis (**Figure 2M, 2N**). Oral corticosteroids (Prednisone, 0.5 mg/kg/day) and oral itraconazole capsules (3.5 mg/kg/day) were administered and his symptoms, peripheral eosinophilia, and high IgE levels improved and his chest CT abnormalities cleared up completely (**Figure 2E, 2F**). The patient was considered to be in complete remission and therefore his oral prednisone and itraconazole were tapered down and to a maintenance dose of 0.07 mg/kg/day and 1.8 mg/kg/day, respectively. No toxicities attributable to the drugs were observed during the 18-month follow-up period.

Literature review

PubMed was searched for articles covering the period from May 1971 to September 2015, using the following search criteria: "allergic bronchopulmonary aspergillosis or ABPA not cystic fibrosis" together with the filter "child". The search was limited to human studies published in English that included treatment strategies for ABPA. The abstracts of all articles were used to confirm the target population and the corresponding full text articles were reviewed. Two investigators independently identified the eligible studies. Any inconsistencies between the two investigators in interpretation of the data were resolved by consensus. A quality assessment of the included studies was performed independently by two of the authors using SPSS 20.0 (SPSS, Chicago, IL, USA).

We reviewed clinical characteristics in all non-CF pediatric patients with ABPA, focusing on their treatments. A total of 15 patients (includ-

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Table 2. Summary of treatments for ABPA in children without CF

First author, year	NO. of patients	Sex/Age (yrs)	Asthma	Imaging findings	Prednisone (the starting dose)	Itraconazole (the starting dose)	Anti-IgE use	Clinical improvement	Prednisone discontinued or decreased	Itraconazole discontinued or decreased	Drug side effects	Follow-up duration (yrs)
Raif S, 1977 [16]	1	F/13	Yes	Pulmonary infiltrates	2 mg/kg per day	No	No	Yes	Discontinued after 6 wk	-	No	0
John E, 1981 [17]	4	M/13	Yes	No pulmonary infiltrates	31 mg (mean dose, per day)	No	No	-	-	-	-	-
		M/15	Yes	Central bronchiectasis	20 mg (mean dose, per day) and 20 mg (mean dose, per other day)	No	No	-	-	-	-	-
		F/15	Yes	Pulmonary infiltrates and central bronchiectasis	10 mg (mean dose, per day) and 11 mg (mean dose, per other day)	No	No	-	-	-	-	-
		M/13	Yes	Pulmonary infiltrates	30 mg (mean dose, per day) and 21 mg (mean dose, per other day)	No	No	-	-	-	-	-
Paul A, 1983 [13]	1	F/18	Yes	Pulmonary infiltrates	15-40 mg per day	No	No	Yes	No (wheezing dyspnea occurred when prednisone dose <20 mg per other day)	-	Yes (Mycobacterial chelonae infection)	3
Roy, 1987 [18]	2	M/12	-	Pulmonary infiltrates	Yes (dose is unknown)	No	No	Yes	-	-	-	12
		M/16	Yes	No pulmonary infiltrates	25 mg per other day	No	No	Yes	-	-	-	9
A.SHAH, 2001 [19]	1	F/14	-	Central bronchiectasis	0.5 mg/kg per day	No	No	Yes	Decreased to 0.5 mg/kg per other day and then prednisone was off and on	-	No	≥1
CPT Christopher, 2004 [20]	1	M/13	Yes	Large consolidative processes and diffuse central bronchiectasis	1 mg/kg per day	Yes (dose is unknown)	No	Yes	No	-	No	-
Mihoko, 2009 [21]	1	M/2	Yes	Pulmonary infiltrates	2 mg/kg per day	No	No	Yes	-	-	No	-
Sunil K, 2009[22]	2	M/4.5	Yes	Not remarkable	1 mg/kg per day for 2 wk	No	No	Yes	1 mg/kg per other day	-	No	-
		F/12	Yes	Fleeting opacities	1 mg/kg per day	No	No	Yes	-	-	No	-
Our cases	2	M/17	Yes	Pulmonary infiltrates and central bronchiectasis	Methylprednisolone, (0.4 mg/kg per day)	0.5 ml/kg per day	No	Yes	Methylprednisolone (0.06-0.1 mg/kg per day)	0.3 ml/kg/day	No	1
		M/15	Yes	Pulmonary infiltrates and a finger sign	0.5 mg/kg per day	3.5 mg/kg per day	No	Yes	Decreased to 0.07 mg/kg per day	1.8 mg/kg/day	No	1.5

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ing our 2 patients) were involved. All 15 children were treated with oral systemic corticosteroids. Prednisone was most often used, while methylprednisolone was prescribed in one of our cases. The total dose of corticosteroids varied depending on the children's weight. The mean equivalent prednisone dose ranged from 0.3 to 2 mg/kg per day in the initial stage. Corticosteroids were tapered down gradually when the children showed clinical improvement. Although prednisone was successfully discontinued after 6 weeks in one child (1/7, 14.3%), most patients required maintenance (5/7, 71.4%) or intermittent (1/7, 14.3%) systemic corticosteroid therapy. Besides corticosteroids, 3 children (3/15, 20%) received adjuvant treatment with itraconazole. No patients were treated with anti-IgE targeted therapy. Mycobacterial chelonae infection caused by a long course of corticosteroids therapy was reported in one case. Thanks to close follow-up, the infection was promptly identified, and the child was treated properly. Other important information is listed in **Tables 1** and **2**.

Discussion

ABPA is a disease resulting from an abnormal host immune response to Af. It was first described by Hinson and Coworkers in 1952 [7]. The familial occurrence of ABPA is around 4.9% [8]. Several genetic characteristics have been identified to explain the differences in disease incidence in the general population: HLA-DR2, HLA-DR5, IL-10 promoter polymorphisms and surfactant protein polymorphisms increase the susceptibility of the disease, while HLA-DQ2 protects against it [9].

Asthma was found to occur in children with ABPA without CF in 13/15 patients, suggesting that there is a very tight correlation between asthma and ABPA without CF in children. Both ABPA and allergic asthma are characterized by a Th2 immune response and therefore the immune response to Af may contribute to the high incidence of asthma in the ABPA population [10]. Cystic fibrosis is a genetic disease of the CFTR that often affects mucociliary clearance in the lungs. The prevalence of ABPA in CF is also high (8.9%), and it is higher in adults as compared to children (around 10.1% vs. 8.9%) [2]. The diagnosis of CF could not be confirmed in our 2 cases because no mutations were found in the patient's *CFTR* sequencing, and

unfortunately, neither patient underwent a sweat chloride concentration test.

The Rosenberg-Patterson criteria, including 7 primary and 3 secondary criteria, are the most often used criteria to diagnose ABPA. The primary criteria are as follows: (1) asthma, (2) peripheral blood eosinophilia, (3) immediate skin reactivity to Af, (4) precipitating antibodies against Af, (5) elevated serum IgE level, (6) pulmonary infiltrates, (7) central bronchiectasis. And the secondary criteria include: (1) Af in sputum, (2) history of expectoration of brown plugs, (3) late skin reactivity to Af [11]. The diagnosis can be established if the patients present the first six of the seven primary criteria (seropositive ABPA), and the presence of all seven makes the diagnosis certain. Although the secondary criteria are not necessarily required for the diagnosis, it has a higher diagnostic accuracy if the patients present more secondary criteria [11]. The diagnosis of ABPA is difficult in children because on the one hand, the current criteria are poor in specificity and it is unusual for all of the criteria to be present in one child. On the other hand, years are often necessary before the diagnosis is established due to the natural evolution of the disease [12]. Thus many children don't meet the criteria until they reach adulthood. The diagnosis of our 2 cases was made based on their typical history, laboratory findings and radiologic investigations.

A combination of oral corticosteroids and antifungal agents is recommended for patients with ABPA [3]. However, there are still many unknowns about the best way to treat children with ABPA: First, the optimal dose, frequency and duration of oral corticosteroids in children are unknown. According to our case review, low-dose corticosteroid therapy was preferred. There are three common types of oral corticosteroids: prednisone, prednisolone and methylprednisolone and prednisone are the most popular. The current recommendation is to start with a sufficient amount of corticosteroids to control the acute symptoms, followed by tapering down until the minimum chronic dose or tapering to off. The maximum starting dose of prednisone in our review was 2 mg/kg per day, while the most common dose was 0.5-1 mg/kg per day or per other day. But the small sample size may limit its value. In addition, intermittent use of corticosteroids (taking oral corticosteroids every other day instead of daily),

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which can significantly minimize the total dose of corticosteroids, was favored by clinicians during remission. The most challenging part about managing children with ABPA was defining the optimal duration of corticosteroids. A long course of corticosteroid therapy was found to control exacerbations, reduce short-term administration of corticosteroids in ABPA led to a high risk of recurrent pulmonary infiltrates and prevent further pulmonary parenchymal destruction, but many serious side effects, such as immune suppression, diabetes and osteoporosis [6], make corticosteroids undesirable for long-term use. On the other hand, recurrent exacerbations or hospitalizations. In the current data synthesis of the published literature and our case report, it was found that non-CF pediatric ABPA patients benefited more from long-term corticosteroid therapy. In 7 cases with descriptions of treatment outcomes, 6 children received maintenance or intermittent oral systemic corticosteroids therapy, resulting in improved persistent symptoms or fewer exacerbations. In contrast, successful discontinuity of corticosteroids was reported only in one child. Most children suffered from disease recurrence after corticosteroids were stopped, and had to restart the therapy with increased dose of corticosteroids. This probably caused more severe side effects than that of stable long-term low-dose use of corticosteroids.

The second problem is that possible side effects may occur from oral corticosteroids. Mucocutaneous infection was identified in one girl in Paul et al's report [13], indicating the potential for infections with long-term low-dose corticosteroid therapy in ABPA children. In order to minimize the unacceptable adverse effects induced by corticosteroids, close follow-up is of great importance. In addition to monitoring patients for deterioration in symptoms, a combination of X-ray or CT findings, lung function and blood tests are used to help judge if side effects are occurring. This child did well despite the infection and the rapid reduction of the corticosteroid dose led to a significant clinical improvement. Over the next 3 years, this child relied on oral corticosteroids to control ABPA but no further side effects were found.

Another problem is that metabolism of antifungal medicines in children remains poorly understood. As side effects from a combination of antifungals and corticosteroids are less severe

than that of higher dose corticosteroids alone, antifungal agents are often given to reduce the dose of corticosteroids and increase the interval between corticosteroid courses, and have thus been proposed as an alternative treatment for ABPA. The mechanism is to confine the burden of the fungal infection, thus attenuating the intense inflammatory response and preventing subsequent deterioration of lung function. A group of compounds with good activity against *Aspergillus* is the azoles. Of this group, itraconazole and voriconazole are often used in ABPA [14]. Amphotericin B has a good effect on invasive infection with *Aspergillus*. Since this is not absorbed orally, and has high toxicity when given intravenously, it is seldom used in non-invasive *Aspergillus* diseases like ABPA. In our review, itraconazole was used as adjuvant treatment in 3 children who responded poorly to low-dose corticosteroid monotherapy, and this was very successful in treating ABPA. The dosing of itraconazole was variable but was most commonly low-dose. For our 2 patients we used 0.5 ml/kg per day (oral liquid) or 3.5 mg/kg per day (oral capsule) in the initial stage, tapering to 0.3 ml/kg/day (oral liquid) or 0.07 mg/kg per day (oral capsule). Usually antifungal agents are given for at least 3 to 6 months, and the duration of antifungals could be shorter than that of oral corticosteroids.

The elevated total IgE level is an important abnormality in ABPA, and omalizumab, a new, recombinant humanized monoclonal anti-IgE antibody, with potential as a new treatment option for ABPA in both the CF and non-CF populations [6]. But a lack of treatment experiences in children and the high cost greatly limit its clinical application. So far, there have been only 13 ABPA children with CF with or without asthma receiving anti-IgE therapy. Omalizumab was administered in order to either to control recurrent exacerbation of ABPA without using corticosteroids or decrease the dose of maintenance corticosteroids [5]. Most of the children responded well to the omalizumab therapy, indicating anti-IgE therapy is helpful for these ABPA children with CF. However, as anaphylaxis, cardiac and thromboembolic events may occur with the administration of omalizumab, anti-IgE treatment is not uniformly recommended for all ABPA patients [15]. In previous literatures, there were no data shown about the safety or efficacy of anti-IgE targeted therapy in ABPA children without CF. None of the 15 chil-

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dren we found from our literature search received omalizumab therapy, indicating that omalizumab was not important in non-CF pediatric ABPA patients with mild to moderate asthma or without asthma. This may be because the ABPA patients with CF are usually sicker than those without CF, and need a more potent treatment to control the disease. Based on these successful treatment experiences summarized from our 15 children, we believe corticosteroid therapy combined with antifungal agents are effective for ABPA in children without CF and suggest that anti-IgE therapy is not necessary. Therefore, we recommend using this cost-efficient and effective treatment strategy in these children population.

In conclusion, long-term low-dose corticosteroid therapy combined with antifungal agents is effective and safe for non-CF pediatric patients with ABPA. Additional anti-IgE therapy is not necessary. Close monitoring can significantly reduce the risks of serious adverse events. However, it should be noted that the summarized data resulted from non-randomized, unblinded treatment interventions lacking a comparison, placebo-treated group. A double-blind, randomized, placebo-controlled trial is still required to evaluate the value of this treatment strategy for ABPA.

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Disclosure of conflict of interest

None.

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